colonies (collections of more than 40 cells) in the medium within 10 to 21 days.

Drugs to be tested for activity against ovarian carcinoma are added to the cell suspension in three different concentrations. After an hour, the cells are washed and prepared for culture. Colonies from a control and three treated media are counted after 14 days through an inverted phase microscope to determine drug effect.

A quantitative sensitivity index of tumor stem cells to each drug can be determined graphically from linear curves that compare drug concentration with colony survival. For each drug, a limit of sensitivity is selected on the basis of preliminary experimental data, and tumors are classified as sensitive if the area under the curve does not exceed the chosen limit.

Patterns of drug activity in vitro can be correlated with subsequent clinical response and tumor specimens can be obtained serially in some patients, providing an opportunity to study the development of drug resistance. It is hoped that the stem cell assay can be used as an initial guide to appropriate chemotherapy and, also, can obviate the need for treatment with toxic drugs to which the tumor is insensitive. To date, the assay appears predictive of response in about 65 percent of cases and of resistance in about 90 percent.

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Two Mechanisms of Late Decelerations: Reflex and Myocardial Hypoxia

THE CURRENT THEORY that late decelerations are due to fetal hypoxia and are, therefore, ominous, does not explain a number of clinical observations. For example, (1) infants born after a prolonged series of late decelerations, even up to several hours in some cases, are not necessarily depressed (low Apgar scores) or acidotic provided fetal heart rate (FHR) variability has been maintained. (2) Infants born after a positive oxytocin challenge test (or contraction stress test) are not necessarily depressed or acidotic at birth. (3) Early decelerations are thought to be due to fetal head compression. The presumed mechanism is a transient change in cerebral blood flow resulting in vagal discharge due to hypoxia. However, such infants are not depressed or acidotic.

Recent animal experimentation, clinical observation and a review of some decades-old human fetal data support the belief that late decelerations are of two types.

Reflex late decelerations, the first type, are seen when a sudden acute insult, such as maternal hypotension, is superimposed on a previously normally oxygenated fetus. These late decelerations are caused by a decrease in uterine blood flow (with the uterine contraction) that makes it impossible for the fetus to extract sufficient oxygen. The deoxygenated blood is carried from the fetal placenta, through the umbilical arteries to the heart and distributed to the aorta, neck vessels and head. Here the low oxygen tension is sensed by chemoreceptors, and neuronal activity results in a vagal discharge that causes the transient deceleration. The deceleration may be late because of the circulation time from the fetal placental site to the chemoreceptors. Between contractions, oxygen delivery is adequate.

These late decelerations are accompanied by normal FHR variability and, thus, signify normal central (for example, the brain or heart) oxygenation; that is, the fetus is physiologically compensated. Centralization of the fetal circulation, a well-recognized fetal response to moderate asphyxia, results from vasoconstriction of nonpriority organs, such as muscle and gut, and increase or maintenance of blood flow to the vital organs, such as the brain, heart and placenta.

Early decelerations, which are mild in depth and usually associated with normal FHR variability, most likely result from the same mechanism as the reflex vagal late decelerations just described.

The second type of late deceleration is initiated in the same manner as the first type except that the deoxygenated bolus of blood from the placenta is also insufficient to support myocardial action. Direct myocardial hypoxic depression as well as vagal activity result. This type of deceleration is seen with more prolonged asphyxia and is recognized by decreased or absent FHR variability, which signifies fetal decompensation—that is, inadequate fetal cerebral and myocardial oxygenation. This condition is seen most commonly in states of decreased placental reserve, such as preeclampsia, intrauterine growth retardation or following pro-

longed stress (for example, prolonged severe variable or late decelerations).

The first type of late deceleration is best described as a stress pattern, which is usually reversible by appropriate treatment, such as maintenance of maternal blood pressure, avoidance of excessive uterine activity, lateral position to maximize placental blood flow and maternal hyperoxia. The second type of late deceleration should be described as a sinister pattern that requires rapid attempts to alleviate it and, if this fails, expeditious delivery of the fetus.

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